# Future topics in fetal magnetocardiography

P. Van Leeuwen

*Dept. of Biomagnetism, EFMT, Bochum, Germany*

## 1 Introduction

Since the first fetal magnetocardiogram was demonstrated by Kariniemi in 1974 [1], various groups worldwide have explored potential of investigating fetal cardiac activity using biomagnetic sensing systems and have examined the issues involved (for an overview, see [2]). In the past 25 years, fetal magnetocardiograms (FMCG) have been recorded in healthy fetuses as well as in pregnancies involving various pathologies. Some groups have worked on the development of appropriate instrumentation for fetal applications or have modeled fetoabdominal volume conduction. The purpose of this paper is to review the status of fetal magnetocardiography today and to delineate the topics with which we will be preoccupied in the future. The following subjects will be discussed: instrumentation, modeling, data acquisition and analysis in healthy pregnancies, clinical applications and software.

## 2 Instrumentation

One primary goal for the future is the development of systems which allow the examination of the prenatal cardiovascular system under normal healthy conditions as well as the identification of clinically relevant pathologies. The majority of FMCG studies to date have relied on biomagnetometers that were developed for neurological and in some cases cardiological applications [2]. These include single, few and many channel systems which implement magnetometer and 1st or 2nd order gradiometer detecting sensors. Most of these systems operate in shielded environment and noise reduction techniques such as software gradiometers and reference sensors estimating the ambient field have been used.

Although much has been achieved with such systems, the instrumentation requirements for fetal application differ from those for the typical cardiological and neurological settings. One may distinguish between large array and single or few channel systems. The former will be used for basic research, as reference systems and in the comparison between models and real life data. They should have extensive abdominal coverage and low noise characteristics and will use low-Tc technology and shielding for some time to come. Systems that have incorporated many of these features include the 67 channel BTi 1300C and the 151 channel CTF SARA (Fig. 1, A and B).

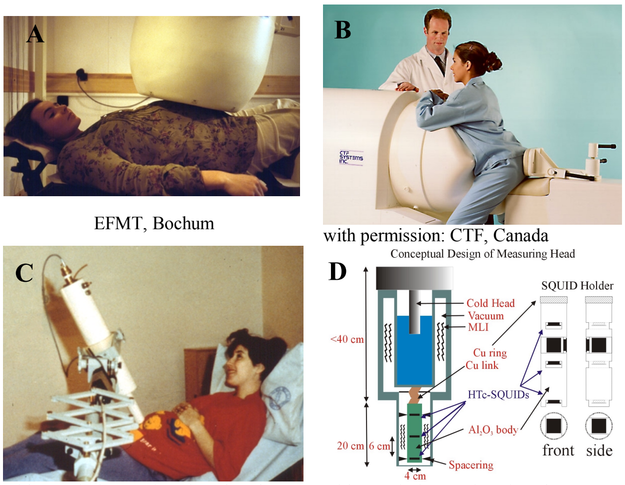

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Figure 1: *Biomagnetometers incorporating features designed for fetal magnetocardiography. A) BTi 1300C: 67 channel magnetometer system with good abdominal coverage and reference coils for noise reduction; B) CTF SARA: 151 channel 1st order gradiometer dedicated fetal biomagnetometer; C) Cryoton (University of Wales): single channel 2nd order gradiometer low-Tc system; D) FHARMON (Dept. Applied Physics, University of Twente): single channel 2nd order gradiometer high-Tc system.*

Single or few channel systems are required for clinical use and thus should be compact and maneuverable high-Tc gradiometer systems. They should operate in an unshielded environment with adequate noise reduction and artifact suppression techniques. To date, some of these requirements have been realized in systems such as the single channel Cryoton (Fig. 1, C). Presently, work is being done in the University of Twente in designing a compact, easy-to-handle system which will help in attaining clinical acceptance (Fig. 1, D). A further development may be the use of 3-D vector systems which can detect signal perpendicular and tangential to the body [3]. This may aid in the determination of the amplitude of the fetal signals more reliably (see below).

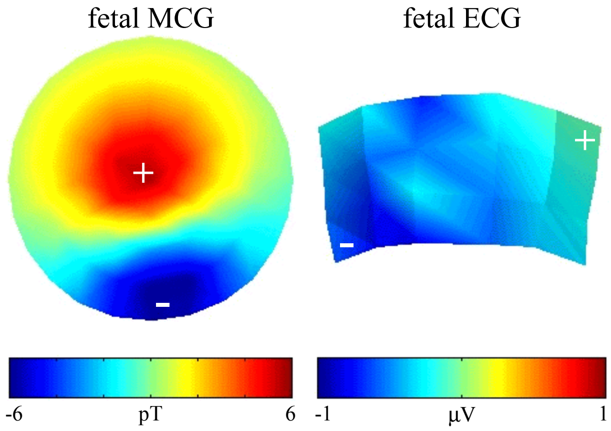

Figure 2**:** *Reconstruction of the magnetic and electric fields at R peak, based multichannel FMCG and FECG recording of a healthy fetus in the 39th week of gestation in the left cephalic position. Note the clear dipolar patter in magnetic field in contrast to the distribution of the electric field. (Image produced by J. Stinstra, Biomagnetic Centre Twente, The Netherlands.)*

## 3 Modeling

Modeling work has also been done to help understand and interpret the signals we are recording. There are a number of topics which have been addressed and which will be the subject of further investigation in the future. These include the type of volume model (simple, realistic), the number and the geometry of compartments which need to be taken into consideration (maternal abdomen, fetal body, placenta, uterus) as well as the conduction pathways and conductivity of the various media. Furthermore the effect of the vernix caseosa, the amount and distribution of amniotic fluid as well as of fetal position, orientation and age must be studied (see e.g. [4]). Calculating the fetal ECG and MCG signals on the basis of models and comparing them to real life data will aid in the refinement of the models. For instance, Fig. 2 demonstrates differences in the FMCG and FECG most likely due to the electrically insulating effects of the vernix caseosa.

## 4 Healthy pregnancies

Numerous studies of fetal magnetocardiography in healthy pregnancies have been published and one may assume that well over one thousand normal FMCGs have been recorded in the second and third trimester to date. This data has been primarily analyzed with respect to cardiac time intervals but also signal amplitude, heart rate variability and the effect of fetal respiratory movements have been investigated [2]. The results have shown that fetal development is reflected i) in the duration and the amplitude of the P wave and the QRS complex (see Fig 3) and ii) in the value of various heart rate variability parameters (see Fig 4). Apart from obtaining a better understanding of fetal physiology, one of the main goals is the determination of parameters which reflect fetal growth and well-being with clinical applications in mind.

To this end, several tasks must be undertaken in the future. Data acquisition and analysis techniques must be improved in order to increase the reliability of the above mentioned parameters. For instance, the timing of the onset and offset of atrial and ventricular de- and repolarization in the FMCG signal is dependent on the position and orientation of the fetus relative to the sensing coil. The correct determination of these times is therefore not only dependent on the signal to noise ratio but also on the adequate positioning of the sensor. This is all the more important for systems with few channels. The estimation of signal amplitude is similarly confoun-

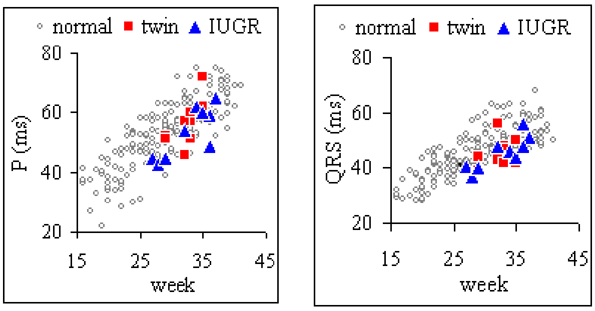

Figure 3**:** *Change in the duration of the P wave and QRS complex in the course of pregnancy in the FMCGs of healthy singleton (n=172), in twin (n=8) and in growth retarded (n=8) fetuses (IUGR: intrauterine growth retardation).*

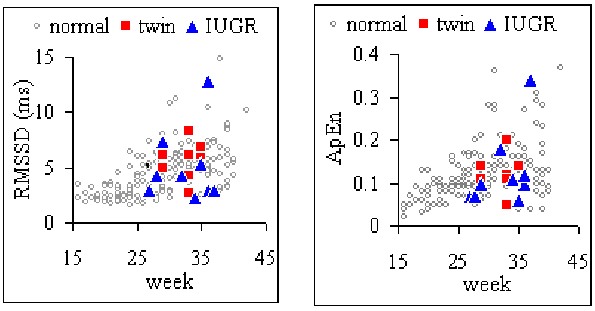

Figure 4**:** *Change in heart rate variability in the course of pregnancyin the same FMCGs as in Fig.3 (RMSSD: root mean square of successive differences; ApEn: approximate entropy).*

ded. Accordingly data acquisition procedures must be established which optimize sensor positioning and data analysis techniques must be developed which reliably estimate the onset and offset of the signals of interest. On the other hand, biomagnetometers such as the 3-D vector system mentioned above may deliver signals with higher information content in this respect.

A further task is the development and application of a common protocol. Such a protocol should take following aspects into consideration:

- anamnestic information on the mother and fetus
- information on fetus at the time of recording
- peri- and postnatal data on the fetus i.e. newborn
- information on instrumentation
- data acquisition parameters
- data analysis procedures.

The setting of standards will allow for dependable high quality data which can then be compared and pooled between groups.

The ongoing acquisition of FMCG in healthy fetuses will increase the reliability of norm data necessary for delineation of pathological states. With this in mind, it will also be necessary to record data in healthy fetuses under defined conditions which take different behavioral states, such as sleep/waking states, respiration, etc., into account. Obtaining a better understanding of the effect of such behavioral states will help explain the variance e.g. of heart rate variability parameters (see e.g. [5]). As can be seen in Fig. 4, such parameters vary over a much wider range in the third trimester and different values may be indicative of different states. In general, the creation of a task force for the establishment of norms and standards is desirable.

## 5 Clinical studies

Compared to the number of reported FMCG acquisitions in healthy pregnancies, there have been relatively few measurements in defined pathologies or in pregnancies with risk. Most of such studies have dealt with the description of a variety of forms of fetal arrhythmia [6]. The analysis of signal morphology for the identification and classification of fetal arrhythmias represents one of the most obvious advantages of fetal magnetocardiography: it fills the diagnostic gap left by the difficulties involved in recording the fetal ECG and highlights the clinical benefits of this simple and non-invasive method. Furthermore, results are now emerging on the effect of intrauterine growth retardation (IUGR) [7,8] and there have been reports on twin pregnancies [9], congenital heart disease [10] and long QT syndrome [11]. The analysis of IUGR data will focus on the shortening of cardiac time intervals as a likely reflection of reduced muscle mass in small fetuses (twin and IUGR data in Fig. 3) and perhaps on heart rate variability as a measure of compromised function (IUGR data in Fig. 4). The application of signal amplitude will depend on the development of methods which ensure its reliable and reproducible determination.

The tasks laid out for the future include the identification of clinically relevant applications. Apart from the above mentioned, these may include cardiac dysfunction and fetal acidosis and distress. On that basis clinical studies, if necessary multicenter, with well-defined goals will need to be conducted. The clinical relevance of the results of such studies will be a determining factor in whether fetal magnetocardiography will attain wide application. In order to achieve this goal, the coordination and collaboration between Biomag groups as well as with clinicians will be of central importance in order to optimize output. One example of such coordination has been the creation of a common database of all data that has been gathered to date with respect to cardiac time intervals [12]: the Biomagnetic Centre Twente in the Netherlands has pooled this data and made it available on the internet (http://bct1.tn.utwente.nl/).

## 6 Software

Prerequisite for the analysis of FMCG data is the availability of appropriate software tools. The signal processing software which is used represents largely tools which have been developed for general biomagnetic applications. These include noise suppression and artifact removal such as software gradiometers and filtering, detection of signal complexes on the basis of spatio-temporal correlation and digital averaging and subtraction of signals. Data analysis techniques specific to fetal application are rare. What is needed are tools which will allow the automatic detection of de- and repolarization events: onset and offset of P-wave, QRS complex, and possibly the T-wave. This will enable the automatic determination of cardiac time intervals. Furthermore, software is required for the quantification of signal amplitude and fetal heart rate variability. The latter should include features which allow data entry and display of RR intervals, (semi-) automatic identification and removal of outliers and ectopic beats, the calculation and display of the frequency spectrum, calculation of heart rate variability parameters from the time, frequency and complexity domains as well as database, printing and exporting functions. Presently, such a tool is being developed in our laboratory [13]. Many of the above mentioned tools should be developed for real-time use in order to facilitate fetal surveillance in the clinical setting.

## 6 Summary

Much has been achieved in the investigation of fetal magnetocardiography over the last decades. One primary goal for the future is the development of systems which allow the examination of the prenatal cardiovascular system under normal healthy conditions as well as the identification of clinically relevant pathologies. The instrumentation requirements for fetal application differ from those for the typical cardiological and neurological settings. In particular, compact, easy-to-handle few-channel systems which can operate in an unshielded environment are necessary to attain clinical acceptance. Modeling work has also been done to help understand and interpret the signals we are recording. Future work will take a more precise geometry of the compartments within the maternal abdomen, their respective conductivities as well as fetal position into account.

Keeping in mind that there are relatively few groups preoccupied with the acquisition of data, a considerable amount of data has been collected to date, most of it in healthy pregnancies. Together with the development of appropriate data analysis techniques, this has allowed for determination of parameters which reflect fetal growth and well-being. In order to utilize this database as a reference in the detection of pathological states, it is necessary to i) increase the number of recordings, particularly with respect to defined behavioral states, ii) establish standards for data acquisition and analysis in order to allow for the pooling of data, iii) further develop the analytic tools in order to refine the conclusions drawn from the data, iv) make the database widely accessible e.g. via the internet.

The main goal will remain the realization of clinical application. The capability of identification and classification of fetal arrhythmias has been demonstrated. However few studies have been done on the utility of fetal magnetocardiography in conditions such as intra-uterine growth retardation, fetal distress or acidosis. Clinical studies on fetuses with well-defined pathologies are indispensable for the development of magnetocardiography as a tool for fetal surveillance.

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